

## Guest Editorial

### Superfund Basic Research Program: A Model for Contemporary Research Programs

Classification of a site as a federal Superfund site triggers a series of onerous legal, technical, and financial obligations for the potential responsible parties. Basic questions such as how dangerous the site is, how clean it has to be made, and the best way to clean it up have no, few, or contradictory answers.

The Superfund Basic Research Program (SBRP) is an organized, innovative, and highly successful federal effort. Given the scope and complexity of cleaning up environmental hazards, the current budget of \$45 million is small, considering the average cost of \$2.3 million for each of the 19 university-based programs, each comprising three to nine research projects and several core facilities. The program at Boston University (Boston, MA), which is typical, includes principal investigators from five departments in three schools (School of Public Health, College of Arts and Sciences, and College of Engineering), two laboratories at the independent Woods Hole Oceanographic Institute, and the Chemistry Department at the University of Missouri. Coordinating such a geographically widespread group is just one of the challenges in operating a successful SBRP, but it is not the most difficult.

The SBRP mandate is to develop methods and technologies to detect and remediate hazardous substances in the environment and to assess their risks to human health using both applied and basic research techniques. These problems are exceptionally tough, but tackling difficult technical and scientific questions—from solving practical and pressing problems to figuring out “how the world works”—is why we went into science. Although the problems are difficult, getting talented scientists to address them is not, if we provide resources and support.

Indeed, one of the great strengths of the SBRP is that it has been able to find world-class basic scientists and include them for the advancement of environmental science. For example, one of the scientists in our program was recognized as an internationally known authority on the peroxisome proliferator-activated receptor (PPAR), which he had been investigating using pharmaceutical agents. When he switched his experimental compounds from drugs to chlorinated ethylenes and then to phthalates (many common xenobiotics are also PPAR agonists), the field acquired a senior investigator who did not need to be trained or retrained and who was immediately productive. After that, the investigator's graduate students also were drawn into environmental science.

Getting top scientists and their students to work on difficult environmental problems is not the challenge. The most difficult challenge lies elsewhere. The SBRP is a research grants program, but like a “centers” program, it requires core facilities and incorporates a community outreach program. Moreover there is a requirement for each program to combine both biomedical and nonbiomedical research, the latter frequently involving engineering aspects of fate and transport of pollutants, their remediation, and relevant basic research. To apply, SBRP applicants must have cross-disciplinary projects, and they have to show collaboration and evidence of “synergy” to stay in the program. This is a very competitive program, with about a one-third turnover at every 5-year cycle.

Real multidisciplinary work, especially when it crosses the divide between biomedical and nonbiomedical disciplines, produces challenges that are rarely recognized. It is naïve to expect



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some kind of magic “chemistry” when scientists from biology and engineering are put together to work on a shared problem. There is not only a technical bridge to cross; there is also a cultural bridge to build.

For example, for a biologist a “model” refers to a model organism such as a mouse. The model retains the full biological complexity of the intended object of study (e.g., a human) but can be manipulated, experimented upon, and studied in ways humans cannot. For a mathematician or a physicist, a model is the logical skeleton of the object of study, stripped of all its extraneous complexity to reveal its underlying simplicity. For biologists, experimental data are the heart of their science. For a mathematical modeler, data are imperfect, noisy shadows of a deeper reality. Finally, physical and mathematical modelers are often psychologically satisfied with an outcome that says a mechanism “could explain” a phenomenon (like periodicity). The interest of the biologist, however, is firmly fixed on an outcome that does explain it.

Biologists and epidemiologists do use mathematics and computers, but they view both as they would any other tool of observation, like a mass spectrometer or a gel. Computers and mathematics do not define scientificity for biologists or epidemiologists—observation and analysis of empirical data do. A corollary is that differential calculus does not guarantee reliable results because the assumptions involved in the model might not be valid. For a biologist or epidemiologist, common assumptions of physicists or mathematicians, such as homogeneous mixing and smooth functions, do not make an analysis tractable; they make it suspect.

This unrecognized cultural difference in outlook has escaped our attention partially because many of our “interdisciplinary collaborations” are with colleagues in other disciplines of biology who share our cultural biases. The good news is that producing shared perspective between biomedical and nonbiomedical scientists, while a genuine challenge, is possible, and the SBRP mechanism has been able to facilitate it. SBRP programs are funded for 5 years at a time, with more than two-thirds renewed for an additional 5 years at the end of each cycle. Thus, researchers may work together on a common set of projects for 5, 10, or 15 years. Moreover, the requirement for cross-disciplinary work creates both the setting and a substantial incentive.

At the same time, biology is changing. Molecular biologists are faced with an unprecedented quantity of data as a result of new technologies requiring the use of advanced computational techniques from unfamiliar areas of mathematics such as computer science, knot theory, and graph theory, whereas proteomics requires combinatorial geometry, thermodynamics, and other areas of physics and chemistry. Biologists have become more receptive to the value of mathematics, and mathematicians, engineers, and computer scientists find themselves on the ground floor of exciting new developments that can be phrased and approached in ways they find congenial. The computer, too, has become more than a number cruncher. Like the microscope, it is also a means to visualize information.

For 15 years the SBRPs have been a model venue to develop and gestate new relationships of this kind. The key elements are time, resources, the requirement to work together, and the incentive to be

productive in the effort. The biology of the 21st century will be a very different kind of biology, comprising many elements that were formerly the province of distant disciplines. The SBRP mechanism somehow—foresight, luck, or both—anticipated this. It has been enormously productive in terms of scientific publication and the development of innovative technologies as a result. Unusually good program management at the National Institute of Environmental Health Sciences (NIEHS) has mitigated the effects of the program's obvious underfunding. The SBRP is a model contemporary program for bringing to bear the best science in aid of both immediate concerns and long-term needs. It is a jewel in the crown of the NIEHS.

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**National Institutes of Health (NIH)**

**National Institute of Environmental Health Sciences (NIEHS)**

**National Human Genome Research Institute (NHGRI)**

**National Institute of Alcohol Abuse and Alcoholism (NIAAA)**

Announces a symposium on:

## **Genetic Variation and Gene x Environment Interaction in Human Health and Disease**

**April 16, 2003; 8:30 am–12:30 pm**

**Masur Auditorium, NIH Campus, Bethesda, MD**

### **Objective:**

This symposium is linked to the *Scientific Symposium: From Double Helix to Human Sequence – and Beyond*, April 14–15 on the NIH Campus (Natcher Center). It will provide an opportunity for in-depth consideration of DNA variation. Talks on the future use of DNA variation in gene x environment interaction research and its implications to human disease will be presented.

### **Scheduled Presentations:**

- DNA Variations and Phylogenetic Considerations – An Overview
- SNPs and Haplotype Blocks/Whole Genome Approaches
- Influence of DNA Variation on Gene Expression
- Relating Variation to Phenotype
- Monogenic Variation and Single Agent Exposure Including G x E Interaction
- Complex Traits/Strategic Approaches
- Future Use of DNA Variation in G x E Interaction Research on Complex Traits

The symposium is open to the public and there is no registration fee. For more information and to register for the symposium go to: <http://www-apps.niehs.nih.gov/odconfer/gxe/home.htm>

Or contact David Brown, NIEHS (919-541-5111) [Brown4@niehs.nih.gov](mailto:Brown4@niehs.nih.gov)